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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/576,527	05/01/2007	Susan Kalled	08201.0042-00000	3828

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BIOGEN IDEC / FINNEGAN HENDERSON, LLP
901 NEW YORK AVENUE, NW
WASHINGTON, DC 20001-4413

EXAMINER

CHANDRA, GYAN

ART UNIT	PAPER NUMBER
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1646

NOTIFICATION DATE	DELIVERY MODE
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02/17/2010

ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No. 10/576,527	Applicant(s) KALLED ET AL.	
	Examiner GYAN CHANDRA	Art Unit 1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 01 September 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-16 and 30-33 is/are pending in the application.
- 4a) Of the above claim(s) 7 and 9-14 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-6, 8, 15, 16 and 30-33 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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DETAILED ACTION

It is noted to Applicant that upon a telephonic interview on 2/3/2010 attorney Nathaniel S. Edwards, the finality of the office action mailed on 11/23/2009 has been withdrawn and prosecution on the merits continues. The instant Office Action is identical to that mailed on 11/23/2009.

Election/Restrictions

Applicant's election without traverse of Group I (claims 1-6, 15, 16 and 30-33) in the reply filed on 9/1/2009 is acknowledged.

Status of Application, Amendments, And/Or Claims

The amendments of claims 1 and 30-32 have been made of record.

Claims 1-16 and 30-33 are pending. Claims 7 and 9-14 are withdrawn.

Claims 1-6, 8, 15, 16 and 30-33 are under examination.

Response to Arguments

Claim Objections/Rejections-withdrawn

Claim Objections

The objection of claims 1 and 30-32 for reciting a non-elected invention (a soluble BAFF receptor) is withdrawn in view of applicants' amendments to claims 1 and 30-32 filed on 9/1/2009.

Claim Rejections - 35 USC § 112-written description-withdrawn

The rejection of claims 1-6, 8, 15-16, 18, and 30-33 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement is withdrawn in

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view of Applicants' amendment of claims 1 and 30-32 to recite a SEQ ID NO: 1 filed on 9/1/2009.

Rejections-maintained

Claim Rejections - 35 USC § 112- enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-6, 8, 15-16, 18, and 30-33 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating a patient having an autoimmune disease comprising an antibody that specifically binds to the polypeptide of SEQ ID NO: 2, does not reasonably provide enablement for treating any immunological disorder comprising administering an antibody that binds to the polypeptide of SEQ ID NO: 2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to which the invention commensurate in scope with these claims.

In *In re Wands*, 8USPQ2d, 1400 (CAFC 1988) page 1404, the factors to be considered in determining whether a disclosure would require undue experimentation include: (1) Nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence of working examples, (6) the breadth of the claims, (7) the quantity of experimentation needed, (8) relative skill of those in the art.

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The instant disclosure fails to meet the enablement requirement for the following reasons:

The claims are broadly drawn to a method of treating a patient having any immunological disorder by administering to the patient a therapeutically effective amount of any antibody that binds to SEQ ID NO: 1.

Applicants argue (see pg. 10-13 of Response filed on 3/12/2009) that it has been established in the art that BAFF antagonists could be used to treat immunological disorders. They argue that the SNF1 mouse is well-established model of systemic lupus erythematosus (SLE) and that the model closely mimics many important features of SLE and applicant cites references Kang et al (2005) and Kalled et al (1998) in support. They argue that short-term administration of a BAFF antagonist to nephritic SNF1 mice results in a long-term clinical benefit (Example 1). They argue that short-term administration of a BAFF antagonist also inhibited cardiac inflammation (Example 3), B cell hyperplasia (Example 4), and production of autoantibody (Example 5) and reduced the percentage of IgMlgD+ B cells which is presumed to be pathogenic (Example 6).

Applicants' arguments have been fully considered but they are not persuasive because the claims are broadly drawn to a method of treating a patient having any immunological disorder by administering to the patient a therapeutically effective amount of any antibody that binds to SEQ ID NO: 1. The claims are not drawn to treating a patient having nephritis or inflammation due to higher blood level of BAFF by administering an antibody that specifically binds to BAFF-R of SEQ ID NO: 2. The specification teaches that the administration of BAFFR-Fc fusion can increase survival

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of mice having nephritis (Example-1) or inhibits cardiac inflammation in SNF1 mice (Example 3). The specification does not disclose any example where the administration of an antibody which simply binds to BAFFR of SEQ ID NO: 1 can treat any immunological disorder.

The specification on pg. 13 discloses that the term "immunologic disorder" refers to disorders and conditions in which an immune response is aberrant. The aberrant response can be due to (a) abnormal proliferation, maturation, survival, differentiation, or function of immune cells such as, for example, T or B cells. Example of immunologic disorders include, but are not limited to, rheumatoid arthritis, asthma, psoriasis, multiple sclerosis (MS), inflammatory bowel disease (IBD), Crohn's disease, systemic lupus erythematosus (SLE), type I diabetes, Wegener's granulomatosis, transplant rejection, graft-versus-host disease (GVHD), hyperproliferative immune disorders, autoimmune diseases, B cell cancers, immuno-modulation, antibody-mediated pathologies (e.g., ITGP, myasthenia gravis, and the like), and Sjogren's syndrome. The specification does not disclose how one skill in the art can treat any immunological disorder by simply administering an antibody which has to only bind to the SEQ ID NO: 1. Ruben et al (US Patent No. 7,112,410) teach a protein TR21 which belongs to TNF family that has 98% sequence homology with the instant protein (see Result 2 for issued patents in SCORE) and teach administering an antibody against TR21 in a person for treating a number of autoimmune diseases using anti-TR21 antibody (col. 122, lines 8+). But Ruben et al does not teach that any antibody that binds TR-21 can treat any autoimmune disease. Similarly, Ambrose et al (US Patent No. 7,112,421) teach a BAFF receptor of SEQ ID

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NO: 5 which is 99 % identical to the instantly claimed invention (see Result 1 for issued patents in SCORE) and a method of treating autoimmune conditions using an antibody against BAFF-R (abstract, col. 5, lines 42+). Therefore, the art teaches that one of the skill in the art would use a specific antibody against the polypeptide of SEQ ID NO: 1 to reduce or ameliorate an autoimmune disease which is associated with such polypeptide but one skilled in the art would be unable to practice the invention as broadly claimed without undue experimentation.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein

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were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-6, 8, 15-16, 18, and 30-33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ruben et al. (US Patent No. 7,112,410) in view of Brenner et al (US Patent No. 5,445,940).

The instant claims are broadly drawn to a method of treating a patient having an immunologic disorder, comprising: (a) administering to the patient a therapeutically effective amount of an antibody that binds to SEQ ID NO:1, at least once or at one or more intervals of less than N weeks; (b) temporarily discontinuing the administration of step (a) for N weeks or longer; and (c) repeating steps (a) and (b) at least once; wherein N is 8, 9, 10, 11, or 12 (claims 1, 30-33), wherein the administration of step (a) comprises an interval of 1,2, 3, 4, 5, 6, or 7 weeks (claim 2), wherein the antibody is administered in step (a) 2, 3, 4, 5, 6, or 7 times a week (claim 3), wherein the administration is discontinued in step (b) for 12, 18, 24, 30, 36, 42, 48 weeks or longer (claim 4), wherein the patient has abnormal titer of autoantibodies in the serum (claim 5), wherein the patient is human (claim 6), wherein the immunologic disorder is an autoimmune disorder (claim 15) and wherein the immunologic disorder is systemic lupus erythematosus (claim 16).

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Ruben et al teach a polypeptide TR21 which belongs to TNF family and the polypeptide has 98% sequence homology with the instant protein (see Result 2 of Issued_Patents_AA on 11/24/2008 in SCORE). Ruben et al teach a method of treating a number of autoimmune diseases by administering an antibody against TR21 in a person for treating (col. 122, lines 8+). They teach that said diseases include lupus associated diseases or disorders, arthritis, nephritis associated with systemic lupus or renal disorders (col. 122, lines 45+) or B cell lineage related cancers (col. 126, lines 3+). It is well known in the art that a person having an autoimmune disease has abnormal level of autoimmune antibodies in the serum. Additionally, regarding the limitation "wherein N is 8, 9, 10, 11, or 12" is routine in the art in the field of STI.

Ruben et al do not teach a method of temporarily discontinuing administration of said antibody for N weeks or longer, and then repeating the treatment.

Brenner et al teach treating an autoimmune disease, rheumatoid arthritis (RA) by administering anti-Val12.1 antibodies (col. 15, lines 36+). They teach the treatment regimens can be by a bolus administration or continuous administration followed by repeated treatment by interruption intervals of three days to couple of weeks as the severity of disease (col.17, lines 15+). It is well known in the art that interruption of treatment would reduce cost to patient and toxicity associated with the treatment.

Therefore, it would have been prima facie obvious to one of the skill in the art to administer an antibody against TR21 which would bind to the polypeptide of SEQ ID NO:1 for treating an autoimmune disease as taught by Ruben et al in a structured treatment interruption format as taught by Brenner et al. One of the skill in the art would

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have been motivated to administer an antibody in a patient having an autoimmune disease as taught by Ruben et al wherein the treatment is at an interval depending on severity of a disease as taught by Brenner because interruption in treatment would reduce cost and toxicity associated with the treatment to said patient. One of the skill would have a reasonable success in administering an antibody against TR21 for treating an autoimmune disease because Brenner teaches treating RA by administering an antibody at an interval of two weeks.

Claims 1-6, 8, 15-16, 18, and 30-33 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ambrose et al (US Patent No. 7,112,421) in view of Brenner et al (US Patent No. 5,445,940).

The instant claims are broadly drawn to a method of treating a patient having an immunologic disorder, comprising: (a) administering to the patient a therapeutically effective amount of an antibody that binds to SEQ ID NO:1, at least once or at one or more intervals of less than N weeks; (b) temporarily discontinuing the administration of step (a) for N weeks or longer; and (c) repeating steps (a) and (b) at least once; wherein N is 8, 9, 10, 11, or 12 (claims 1, 30-33), wherein the administration of step (a) comprises an interval of 1, 2, 3, 4, 5, 6, or 7 weeks (claim 2), wherein the antibody is administered in step (a) 2, 3, 4, 5, 6, or 7 times a week (claim 3), wherein the administration is discontinued in step (b) for 12, 18, 24, 30, 36, 42, 48 weeks or longer (claim 4), wherein the patient has abnormal titer of autoantibodies in the serum (claim 5), wherein the patient is human (claim 6), wherein the immunologic disorder is an

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autoimmune disorder (claim 15) and wherein the immunologic disorder is systemic lupus erythematosus (claim 16).

Ambrose et al teach a polypeptide BAFF-R which has 99% sequence homology with the instant protein (see Result 1 of Issued_Patents_AA on 11/24/2008 in SCORE). Ambrose et al teach using an antibody against TAFF-R for treating autoimmune conditions (abstract, col. 5, lines 42+). They teach treating autoimmune conditions such as systemic lupus erythematosus, rheumatoid arthritis, Grave's disease, or B cell carcinomas (col. 5, lines 50+). It is well known in the art that a person having an autoimmune disease has abnormal level of autoimmune antibodies in the serum. Additionally, regarding the limitation "wherein N is 8, 9, 10, 11, or 12" is routine in the art in the field of STI.

Ambrose et al do not teach a method of temporarily discontinuing administration of said antibody for N weeks or longer, and then repeating the treatment.

Brenner et al teach treating an autoimmune disease, rheumatoid arthritis (RA) by administering anti-Val12.1 antibodies (col. 15, lines 36+). They teach the treatment regimens can by a bolus administration or continuous administration followed by repeated treatment by interruption intervals of three days to couple of weeks as the severity of disease (col.17, lines 15+). It is well known in the art that interruption of treatment would reduce cost to patient and toxicity associated with the treatment.

Therefore, it would have been prima facie obvious to one of the skill in the art to administer an antibody against TAFF-R which would bind to the polypeptide of SEQ ID

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NO:1 for treating an autoimmune disease as taught by Ambrose et al in a structured treatment interruption format as taught by Brenner et al. One of the skill in the art would have been motivated to administer an antibody taught by Ambrose et al for treating an autoimmune disease, wherein the treatment is at an interval depending on severity of a disease as taught by Brenner because interruption in treatment would reduce cost and toxicity associated with the treatment to said patient. One of the skill would have a reasonable success in administering an antibody against TAFR for treating an autoimmune disease because Brenner teaches treating RA by administering an antibody at an interval of two weeks.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to GYAN CHANDRA whose telephone number is (571)272-2922. The examiner can normally be reached on 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol can be reached on (571) 272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

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Status information for unpublished applications is available through Private PAIR only.

For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Gyan Chandra
AU 1646

/Robert Landsman/
Primary Examiner, Art Unit 1647